

In the Specification:

Please replace the paragraphs on page 39, line 4 to page 41, line 9 with the following rewritten paragraphs:

Figure 15. Engraftment and Survival of Human Stro<sup>bright</sup> Cells Injected Into Rat Tumors. Athymic nude rats were irradiated with 250 Gy for 5 minutes to remove residual natural killer function, then injected subcutaneously in the flank with  $1 \times 10^6$  rat glioblastoma cells. Two weeks after implantation, the glioblastoma tumors were directly injected with either 500,000 Stro<sup>bright</sup> cells, 500,000 Stro<sup>dim</sup> cells or saline, and animals were sacrificed 7 days later. In 2/3 tumor tissues which received Stro<sup>bright</sup> cells, staining by immunoperoxidase method using a monoclonal antibody with specific reactivity against human, but not rat, mitochondria, demonstrated numerous human cells around the injection site, indicating medium-term engraftment and survival. Human cells were not detected in any of the three tissues receiving Stro<sup>dim</sup> cells, suggesting that ~~Stro<sup>bright</sup>~~ Stro<sup>bright</sup> cells might have a survival or replicative advantage in this *in vivo* model system (see panel A). The Stro<sup>bright</sup> cells were predominantly in clusters nearby small capillaries and arterioles (small arrows) (panel B). In addition, several human cells were seen to incorporate into vascular structures (large arrow) (panel C). These data indicate that human Stro<sup>bright</sup> cells can both induce neovascularization of endogenous (rat) vessels and can become incorporated into new vessels of human origin.

Figure 16 2. Induction Of Tumor Neovascularization (Angiogenesis And Arteriogenesis) By Human Stro<sup>bright</sup> Cells. In consecutive sections of the tumor tissue stained by immunoperoxidase method using monoclonal antibodies directed, respectively, against von Willebrand Factor (vWF) and alpha-smooth muscle actin (alpha-SMA), animals injected with Stro<sup>bright</sup> cells demonstrated significantly greater numbers of capillaries and arterioles (defined, respectively, by vWF staining alone and combined expression of vWF and alpha-SMA) than animals injected with saline.

Figure 17 3. Stro<sup>bright</sup> Cells Are More Potent Inducers Of Neovascularization (Angiogenesis And Arteriogenesis) Than Stro<sup>dim</sup> Cells. Quantitation of arteriolar numbers (defined as vascular structures with lumen diameter > 50 microns and circumferential expression of alpha-SMA) demonstrated that animals injected with Stro<sup>bright</sup> cells had almost eight-fold greater number of arterioles than saline-treated controls at the site of injection ( $40 \pm 5$  vs  $6 \pm 2$  arterioles/high power field,  $p < 0.01$ ), while no difference could be detected distal to the injection site. Animals injected with the Stro<sup>dim</sup> progeny demonstrated a modest, two-fold increase in the number of arterioles at the injection site relative to saline-treated controls ( $13 \pm 3$  vs  $6 \pm 2$  arterioles/high power field,  $p < 0.01$ ), indicating that the Stro<sup>bright</sup> progeny contained the most potent pro-arteriogenic cells following *in vitro* culture.

Figure 18 4-. Dose-Dependent Effect Of Stro<sup>bright</sup> Cells On Myocardial Neovascularization. To examine whether induction of angiogenesis and arteriogenesis could be extended to other tissues, and was associated with

biological significance, cultured progeny of Stro-selected cells were injected by direct intramyocardial injection into the peri-infarct regions of the ischemic hearts in athymic nude rats who had undergone left anterior descending coronary artery (LAD) ligation two days earlier. Animals injected with  $1 \times 10^6$  Stro<sup>bright</sup> cells demonstrated three-fold greater numbers of arterioles at the peri-infarct region than animals injected with saline ( $12 \pm 2$  vs  $4 \pm 1$  arterioles/high power field,  $p < 0.01$ ). In contrast, animals injected with only  $0.2 \times 10^6$  Stro<sup>bright</sup> cells, delivered in a total of  $1 \times 10^6$  unfractionated cultured progeny of Stro-selected cells, induced only 50% greater numbers of arterioles at the peri-infarct region than saline ( $6 \pm 1$  vs  $4 \pm 1$  arterioles/high power field,  $p < 0.05$ ), indicating that Stro<sup>bright</sup> cells have a dose-dependent effect on arteriolar induction in the ischemic heart.

Figures 19, 20 and 21 ~~5, 6 and 7~~. Stro<sup>bright</sup>-Dependent Myocardial Neovascularization Results In Global Improvement of Parameters Of Myocardial Function. We next examined the effects of Stro<sup>bright</sup>-dependent myocardial neovascularization on global parameters of cardiac function. As shown in figure 19~~5~~, injection of about  $0.1 - 0.2 \times 10^6$  and  $1 \times 10^6$  Stro<sup>bright</sup> cells resulted in dose-dependent improvement in ejection fraction (EF) at 2 and 6 weeks, as measured by echocardiography performed and analyzed by a blinded technician. Animals receiving  $1 \times 10^6$  Stro<sup>bright</sup> cells demonstrated mean improvement in EF at 2 and 6 weeks of 50% and 75%, respectively, relative to baseline values two days post-LAD ligation. In stark contrast, saline-treated animals showed only 5% mean improvement in EF by 6 weeks ( $p < 0.01$ ), and animals treated with

Applicants: Stan Gronthos and Andrew Zannettino  
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Stro-depleted fresh bone marrow mononuclear cells demonstrated no difference compared with those receiving saline. Injection of  $1 \times 10^6$  Stro<sup>bright</sup> cells resulted in similar dramatic improvement in fractional area shortening (FAS) (mean improvement of 70% and 90% at 2 and 6 weeks, respectively, figure 20 6). Stro-depleted bone marrow mononuclear cells again had no effect, while modest improvement was seen after injection of about  $0.1 - 0.2 \times 10^6$  Stro<sup>bright</sup> cells. Finally, as shown in figure 21 7, injection of  $1 \times 10^6$  Stro<sup>bright</sup> cells resulted in significant improvement in left ventricular compliance compared with saline-treated controls. Animals receiving Stro<sup>bright</sup> cells demonstrated over 50% reduction in both left ventricular mean end-diastolic pressure and diastolic pressure (each  $p < 0.01$ ), and over two-fold improvement in  $dp/dt$  ( $p < 0.01$ ). Together, these results indicate that the neovascularization (angiogenesis and arteriogenesis) of ischemic rat myocardium induced by injection of  $1 \times 10^6$  human Stro<sup>bright</sup> cells resulted in significant improvement in both global systolic and diastolic parameters of cardiac function.

Please replace the paragraph on page 41, line 22 to page 41, line 32 with the following rewritten paragraph:

In the first series of experiments, semi-quantitative RT-PCR analysis was employed to examine the gene expression profile of various lineage-associated genes present in the cultured MPC populations (Figure 23 15). Relative gene expression for each cell marker was assessed with reference to the expression of the house-keeping gene, GAPDH, using ImageQuant software (Figure 23B 15-B). In addition, single-colour flow cytometric analysis was used to examine the protein

expression profile of ex vivo expanded MPC based on their expression of cell lineage-associated markers (Figure 23A ~~15-A~~). A summary of the general phenotype based on the gene and protein expression of the cultured MPC is presented in Table 1. Direct comparison of the gene expression profile of MPC described in the present patent demonstrated clear differences between this cell population and mesenchymal stem cells (MSC) previously described by Pittenger et al. 1999, (Table 1).

Please replace the paragraph on page 42, line 27 to page 43, line 3 with the following rewritten paragraph:

Figure 22 ~~23~~. Ex vivo expanded STRO-1<sup>bri</sup> MPC can develop into arterioles *in vitro*. Single cell suspensions of ex vivo expanded bone marrow STRO-1<sup>bri</sup> MPC were prepared by trypsin/EDTA treatment then plated into 48-well plates containing 200µl of matrigel. The STRO-1<sup>bri</sup> MPC were plated at 20,000 cells per well in serum-free medium (Gronthos et al. 2003) supplemented with the growth factors PDGF, EGF, VEGF at 10ng/ml. Following 24 hours of culture at 37°C in 5% CO<sub>2</sub>, the wells were washed then fixed with 4% paraformaldehyde. Immunohistochemical studies were subsequently performed demonstrated that the cord-like structures expressed alpha-smooth muscle actin identified with a goat-anti-murine IgG horse radish peroxidase antibody.